

**Amendments to the Specification:**

Please replace the paragraph at column 5, lines 14-15 with the following amended paragraph:

FIG. ~~11~~18 is a block diagram of the method for determining the attenuation and the intrinsic fluorescence of a sample;

Please replace the paragraph at column 5, lines 16-19 with the following amended paragraph:

FIG. ~~12~~19 is a graph of the attenuation spectrum measured from normal and ischemic renal cortex of rabbit kidney using LIFAS devices and methods in accordance with the invention;

Please replace the paragraph at column 5, lines 20-23 with the following amended paragraph:

FIG. ~~13~~20 is a scatter plot of the fluorescence intensity at 480 nm acquired from hypoxic (+), normal (o) and hyperoxic (x) tissue through excitation-collection and collection-only waveguides;

Please replace the paragraph at column 5, lines 24-26 with the following amended paragraph:

FIG. ~~14~~21 is a graph of the intensity  $I_{co}(\lambda)^c$  of the signal measured by a collection-only waveguide from normal, hyperoxic and hypoxic tissue;

Please replace the paragraph at column 5, lines 27-28 with the following amended paragraph:

FIG. ~~15(a)~~22(a) is a graph of the modulated LIF spectra of normal and ischemic kidney, and

Please replace the paragraph at column 5, lines 29-30 with the following amended paragraph:

FIG. ~~15(b)~~22(b) is a graph of the intrinsic LIF spectra of normal and ischemic kidney;

Please replace the paragraph at column 5, lines 31-33 with the following amended paragraph:

FIGS. ~~16(a) and (b)~~23(a) and (b) are graphs of typical modulated LIF spectra of normal and ischemic kidney, respectively, depicting the difference in the symmetry of the main lobe; and

Please replace the paragraph at column 9 lines 25-46 with the following amended paragraph:

The method of determining the attenuation and intrinsic fluorescence of a sample is better understood with reference to the block diagram shown in FIG. ~~14~~18, which illustrates the main steps involved in determining the wavelength-dependent attenuation coefficient  $\alpha(\lambda)$  and the intrinsic fluorescence  $I_T(\lambda)$  of a sample in accordance with the current invention. In the embodiment shown in FIG. 2(a), the first and second portions **228** and **230** of the return light **220** experience different attenuation effects due to the unequal path lengths traversed by the return light **220** from the sample volume **213** to the apertures **221a** and **222a** of the collection waveguides **221** and **222**. The first portion **228** of the return light **220** collected by the aperture **221a** travels an additional path-length of  $\{y_1'-y_2'\}$  through the tissue as compared to the second portion **230** of the return light **220** which is collected by the aperture **222a**. Hence, the first portion **228** of the return light **220** suffers more path-length-dependent attenuation as compared to the second portion **230** of the return light **220**. Thus, the signals **224a** and **225a** representing the intensity  $I_{c1}(\lambda)$  and  $I_{c2}(\lambda)$  at different wavelengths will exhibit differing levels of modulation caused by the attenuation of the sample **214**.

Please replace the paragraph at column 18, lines 5-18 with the following amended paragraph:

The LIFAS-derived LIFA spectra of normal and ischemic rabbit kidney are shown in FIG. ~~12~~19. The LIFA spectra shown in FIG. ~~12~~19 are acquired using a LIFAS system employing

308 nm excitation radiation produced by an XeCl excimer laser. This LIFAS system uses a 335 nm longpass filter (Schott WG335) to cutoff backscattered excitation radiation from the collected return light. Hence, for this particular LIFAS system the LIFA values below 350 nm are not reliable. For biological tissue, the LIFA values in the wavelength band about 480 nm have the highest signal-to-noise ratio and hence measurement accuracy. As shown in FIG. ~~12~~19, the LIFA of ischemic tissue is lower than the LIFA of normal tissue over the entire spectrum and is particularly low in the region from 350 to 450 nm.

Please replace the paragraph at column 18, lines 19-29 with the following amended paragraph:

As demonstrated in FIG. ~~12~~19, the LIFA, absorbance or percent transmittance at a predetermined wavelength or wavelength bands can be used for the detection of ischemia or hypoxia. Furthermore, predictive models, spectral recognition techniques and associated classifiers can be applied to identify whether a given LIFA, absorbance or percent transmittance spectrum has been acquired from normal, ischemic or hypoxic tissue. The classifiers can be initially trained with LIFA, at a predetermined wavelength or wavelength bands acquired from tissue with a known state of perfusion or oxygenation.

Please replace the paragraph at column 18, lines 30-57 with the following amended paragraph:

Another parameter found to be useful in the classification of normal, ischemic and hypoxic tissue, is the intensity of return light from a pair of LIFAS collection pathways (i.e.,  $[I_{c1}(\lambda)^c, I_{c2}(\lambda)^c]$  or  $[I_{xc}(\lambda)^c, I_{co}(\lambda)^c]$  for the LIFAS embodiments described above). For example, FIG. ~~13~~20 shows the  $[I_{xc}(\lambda)^c, I_{co}(\lambda)^c]$  pair at  $\lambda=480$  nm, symbolized as  $[I_{xc}(480)^c, I_{co}(480)^c]$ , measured from hyper-oxygenated (x), normal (o) and oxygen deficient (+) rabbit kidney. The  $[I_{xc}(480)^c, I_{co}(480)^c]$  from normal and oxygen deficient tissue tend to cluster in two linearly separable regions of the two dimensional  $I_{xc}(\lambda)^c$ - $I_{co}(\lambda)^c$  space. Thus, a simple linear or nonlinear classifier function can be trained on a set of  $[I_{xc}(\lambda)^c, I_{co}(\lambda)^c]$  pairs measured using a LIFAS system from normal, ischemic and hypoxic tissue. Other classifiers such as artificial neural networks (ANN) are also

being used. The trained classifier function can then be used to classify an unknown  $[I_{xc}(\lambda)^c, I_{co}(\lambda)^c]$  pair as normal, ischemic or hypoxic. A "nearest neighbor" (NN) classifier has been found to perform satisfactorily. The NN classifier checks the proximity of an unknown  $[I_{xc}(480)^c, I_{co}(480)^c]$  pair to clusters of predetermined  $[I_{xc}(480)^c, I_{co}(480)^c]$  pairs measured from known normal, ischemic and hypoxic tissue. Other classifiers such as artificial neural networks (ANN) can also be utilized. For myocardial and renal tissue it has been found that it is preferable to use  $[I_{xc}(\lambda)^c, I_{co}(\lambda)^c]$  measured at 480 nm, to optimize signal-to-noise ratio. However,  $[I_{xc}(\lambda)^c, I_{co}(\lambda)^c]$  at other single or multiple pre-selected wavelengths can also be used.

Please replace the paragraph at column 18, line 58 through column 19, line 15 with the following amended paragraph:

An additional parameter for the classification of normal, ischemic and hypoxic tissue, is the wavelength of the peak transmittance of the tissue, symbolized hereafter as  $\lambda_{\max-T}$ , especially in the 450-500 nm band. An alternative to  $\lambda_{\max-T}$  is the wavelength of the peak  $I_{co}(\lambda)^c$  in the 450-500 nm band, symbolized hereafter as  $\lambda_{\max-co}$ . Both  $\lambda_{\max-T}$  and  $\lambda_{\max-co}$  shift towards shorter wavelengths as the hemoglobin in the tissue becomes deoxygenated. For example, FIG. **1421** shows  $I_{co}(\lambda)^c$  spectra that are acquired using the LIFAS system shown in FIG. 10 employing 308 nm excitation radiation produced by an XeCl excimer laser. It should be noted that the  $\lambda_{\max-co}$  of normal tissue shifts to a shorter wavelength as the tissue becomes hypoxic; whereas the  $\lambda_{\max-co}$  of normal tissue shifts to a longer wavelength as the tissue becomes hyperoxic. Specifically,  $\lambda_{\max-co}$  varies between about 480 and 500 nm as blood or hemoglobin oxygenation varies between deoxygenated to oxygenated, respectively. A separation border can be identified at about 489.5 nm to separate  $\lambda_{\max-co}$  of normal tissue (peaks above 489.5 nm) from hypoxic/ischemic tissue (peaks below 489.5 nm). A simple classifier can be trained to identify tissue as hypoxic if its  $\lambda_{\max-co}$  is below 489.5, and vice versa. The degree of hypoxia is determined from the magnitude of the shift in  $\lambda_{\max-co}$  from the normal value, the smaller the shift the subtle the hypoxia.

Please replace the paragraph at column 19, lines 16-28 with the following amended paragraph: